Table 1. Comprehensive Summary Table on Literature Review of Pentosan Polysulfate

Name	Study Design	Methods	Recruitment Criteria	Sample Size	Efficacy Assesment (Outcome) Measure	Findings
Nickel et al (2015) United States/Canada	Randomized, double-blind, placebo controlled, multicenter study	ICSI was administered at baseline, and at weeks 4, 8, 12, 18 and 24. Patients received PPS once daily, or 3 times daily or a matching placebo for 24 weeks.	Men and Women, 18 years or older, ICSI Total Score of 8 or greater, score of greater than 0 on 4 ICSI component items noy associated to UTI.	368: 36 male, 332 female Mean age - 44.6	Rated IC/BPS symptoms : at baseline, and at weeks 4, 8, 12, 18, 24 using the ICSI Questionnaire. - Success was defined as a 30% reduction in ICSI score. Also used a average bladder tain intensity during previous 3 days using an 11 point numerical scale rating of 0 - 10. PORIS was administered to patients at all visits after baseline to measure pain, urgency and the overall change compared to before study drug initiation. GRA	No statistically significant difference between PPS dose group and placebo group, or between 2 PPS dose groups for the primary end point. 4 point or greater decrease in ISCI - 55 (43.0) #s for ICSI, PORIS, GRA all did not have statistical signifant changes.
Davis et al (2008) United States	Randomized double-blind clinical trial	Patients were randomized to a combination of intravesical PPS + oral PPS or intravesical normal saline + oral pps (placebo) for 6 weeks followed by taking oral PPS for a nother 12 weeks.	Females, older than 18 years, diagnosed with IC within 1 year of the beginning of study, and previously untreated with either intravesical or oral PPS. Cytoscopic examinations under anesthesia, hydrodistension and photo documentation showing petechial hemorrhage or ulcers, negative urine culture, a score of at least 4 on a 9 point pain scale, a 5 on the ICSI and a 4 on the ICPI.	41 females: mean age - 36.9	change from baseline to week 6, 12, and 18 and the severity of symptoms measured by ICSI and ICPI, and total score. PUF questionnaire, pain assessment, urgency scale, and voiding diaries. The SF-36 that measures HRQoL. Sexual function VAS.	Changes in OSS, ICSI, ICPI, PUF, PUF symptom index, PUF bother index, Pain Scale, , Voiding frequency, and Nocturia all saw significant improvement from baseline (all p<0.05) in placebo group (oral only).
Nickel et al (2005) Canada	randomized double-blind, double dummy, parallel group, multicenter 32 week study.	Evaluated 3 dosages (300,600, 900) of PPS in a randomized double-bline, duouble dummy, parallel group multicenter study. Adults were randomized to treatments and completed the PORIS and ICSI at baseline, and during follow-up visits at 4, 8, 12, 16, 24, and 32 weeks.	Adults with a diagnosis of IC as determined by either history of symptoms, combined with bladder pain and urgency. Cytoscopic examination and hydrodistention was conducted 6 weeks prior to enrollment.	309: 278 female, 31 men: mean age - 45	ICSI, PORIS	Response according to PORIS scores confirmed that response to treatment was not dose dependent. Not statistically significant between dosage groups. However, ICSI scores improved from baseline to endpoint for all dosages (p<0.01 for all)
Hanno (1997) United States	open-label physician's usage studystudy	Patients diagnosed who met the study entry criteria received shipments of PPS for 3 months, and would receive the drug provided that they completed and returned questionnaires about their disease symptoms and had laboratory data collected before each new shipment. Patients were required to purchase the medication.	Male and female patients previously diagnosed symptomatically and cystoscopically as suffering from IC.	2809 Patients	No statistical plan for efficacy anlysis included in protocol beyond descriptive statistics. Positive response definitions were chosen post hoc to be consistent with those analyzed in prior double-blind studies. Patients included in statistical evaluation of efficacy were required to have at least 1 reorder of medication, therefore continuing the treatment after the first 3 months. All efficacy assesments were made by patients in terms of descripive statistics for the severity of pain, discomfort, and urgency and for the number of voids per day and per night.	Patients' assesments of overall change in IC symptoms showed that 42% to 62% experienced moderate or better improvement compared to symptoms before elmiron therapy. Overall assessment that pain had improved moderately or beter was reported by 42-62% of patients. Urgency declined in duration-dependent fashion, with a minimum of 35% of responsive patients in the 0-5 month group and maximum of 56% of patients of responsive patients reached by 29 months of treatment or longer. Overall - improvement of symptoms that continues throughout 3 years. (Longer treatment, better improval)
Parsons (1993) United States	Randomized, prospective, double-blind, placebo-controlled study.	Multicentered, double-blinded. Patients were selected and randomly assigned to receive PPS or placebo. Symptomatology and laboratory values were obtained before and 3 months after the start of treatment	basis of anesthetic bladder capacity, number of voids per day (8 or more), average voided volume, and nocturia. Patients lacking 1 or 2 of these criteria could enter study but they had to have pain and/or moderate urgency, negatie urinary cytology studies and cultures, and cystoscopic findings of petechial hemorrhages and bloodin the fluid return after bladder dilation.	148 patients, all women, mean age - 42.7	Follow-up questionnaire completed by patients at end of double blind tretment period.	32% of patients showed significant improvement compared to 16% on placebo (p=0.01). Patrients on drug therapy also experienced significant decrease in pain and urgency (p=0.04 and p=0.01) when compared to placebo. Drug patients showed an average increase of more than 20 mL in voided volume than did placebo patients(p=0.02)
Mulholland (1990) United States	Double-blind with placebo control.	Multicentered, double blinded study. Patients were enrolled and treated for 3 months with PPS. Placebo controlled	Patients had to have following examination requirements and symptom comples: urgency expressed as "moderate" on 5-point analog scale, frequency of at least 10 voids per day, nocturia of at least 2 voids per night, pain as recorded on a 5 point analog scale, continuous duration or symptoms of at least one year, failed preious conventional therapy such as chlorpactin, hydrodilation, or DMSO, average voided volume of 200 ml or less measured over 3-day period, negative urine culture and cytology, cytoscopic examination under anesthesia showing petechial hemorrhages or ulcers with gross blood in fluid return and a bladder capacity of 800 mL or less.	110 patients: 100 women, 10 men - mean age: 43.3	Variables for the determination of efficacy in order of relevancy ewere: the patients assessment of overall improvement, the investigators assessment of overall improvement, the changes in pain and urgency, the change in nocturia, and the change in frequency and average voided volume. In each cas the change from the baseline values at the end of the double-blind period was used as the bais for determining the efficacy of Elmiron.	OVerall improvement 3 months, investigator evaluation: 26% improved, p=0.03 Patient self evaluation - overall improved: 28%, p=0.04 patient follow-up questionnaire - 27%, p=0.08 Pain scale - 46%, p=0.07 Pressure to urinate - 22%, p=0.08 Urgency scale - 39%, ns Mean reduction in pain score from baseline- 0.5, ns **significantly different from 0, p=0.05

Table 1 Continued

Parsons (1987) United States	Double-blind with placebo control	Double-blind fashion study. Multicenter. Patients were enrolled and treated for a minimum of 4 months. Placebo controlled.	Patients were eligible if they had at least 1 year of symptoms consisting of urgency, frequency, nocturia and/or pain. Also required to have negative urine cultures, a cystoscopic examination that showed an ulcer or petechial hemorrhage (after bladder distension), biopsy proved inflammation and negative cytology studies.	62 patients: 55 women, 7 men - age not reported	Subjective improvements were measured with questionnaires with categories of: pain, urgency, frequency and nocturia. Objective improvement was measured with average voided volumes, and frequency of daily and nightly voiding episodes.	Significant subjective improvement was seen for all symptoms. Objective improvement was seen for average voided volumes, but not in the number of voids per day.
Holm-Bentzen (1987) United States	Prospective double-blind clinically controlled multicenter trial	Double-blind fashion study. Multicenter. Placebo controlled. 2 protocals were used. Protocal A included 43 patients with clinically and pathologically anatomically verified interstitial cystitis (28 or more mast cells per mm) and protocol B included 72 patients with a painful bladder and unspecified histological findings.	Patients had clinical and/or cystoscopic evidence of painful bladder disease for at least 1 year and repeated negative urine cultures. In protocol A, the fulfillment of pathological anatomical criterion for IC was necesssary, namely more than 18 mast cells per mm squared in the detrusor muscle in a bladder biopsy. In protocol B, no definite pathological anatomical criteria were obtained, but all patients had mast cell counts less than 28/mm squared. To ensure a certain degree of severity of the disease, patients included in protocol B had to have 3 or more voidings each night and more than 10 points on a defined symptom score scale.	115 patients - all women, median age of 63	Symptomatic evaluation, urodynamic paramaters, cystoscopic appearance and mast cell counts.	No difference between treatment group and placebo groups in both protocol in regard to symptoms, urodynamic parameters, cystoscopic appearance and mast cell counts. Significant increase in the cystoscopically determined bladder capacity in the PPS group in protocol A was found.